BOYLSTON PRIZE ESSAY.

ART. XV.—*Tubercle—its Pathology, and especially its Relation to Inflammation.* By C. ELLIS, M. D., of Boston.

IN the attempt to elucidate the above question, it is not necessary that an exposition should be made of all that has been written upon tubercle. It is only within the last few years that the subject has been properly discussed, and that new and more accurate methods of investigation have been brought to bear upon it. We wish to know, therefore, what ideas prevail with regard to it *now*—the facts of to-day, which necessarily include the real facts of the past.

As the basis for the inquiry into which we are about to enter, we shall endeavour to give as concise a description as possible of tubercle, as it is now regarded by the best observers, such as Virchow, Rokitansky, Lebert, and Paget, limiting ourselves to facts. We shall afterwards consider the real meaning and bearing of these facts, judging them by cases drawn from our own experience and that of others.

The very object of the present essay being to give if possible an idea of the real nature of tubercle, we will not attempt to frame any comprehensive definition at the commencement, but hope to show clearly when our work is done, that much of that which is called tubercle is nothing of the kind, and, perhaps, to show approximately what the peculiar product is.

In the usual descriptions of tubercle its properties are so intermingled, and confounded with accidental appearances that but few gain any precise idea of them. This confusion seems entirely unnecessary, as, like other visible objects, it has some features which are constant—which belong to it, as a tubercle, and these it should be the object of the writer to show, keeping carefully out of sight modifications, which are the result of accident, and which may be alluded to in their proper place. Our first labour must, therefore, be the separation of the materials, which we are to use, in order that each part may find its proper place. In rearranging them, the most natural method to pursue appears to be that of describing, first, the most obvious properties, such as form, colour, consistence; then those which require a more accurate and profound investigation.

Form or Configuration.—We shall first speak of the form, that is, the configuration of tubercle. Now tubercle, unlike a crystal, a plant, or an animal, has no definite form. It is always an infiltration. Its configuration is often the result of accident, and, yet, variations attributable to this have been seized upon and made the basis of subdivisions, which have only added to the previously existing obscurity. To speak practically, however, we meet with it in two forms and two only; one regular, spheroidal, as by growth from a centre; the other irregular, as if the result of infiltration among the tissues. Under these two heads may be classed every variety mentioned.

The nodules in the first form vary in size, from those which are just perceptible to those several inches in diameter. To the smaller, the term tubercle is more applicable, or, at least, more often applied than to the latter, which would probably be spoken of as tubercular collections or tubercular masses; still they have a certain regularity of outline.

In the second form, the product is met with as an infiltration, extending irregularly among the tissues, and often occupying large portions of organs. In connection with these masses will be frequently seen minute points of the same material—a kind of tubercular dust—by the aggregation of which the larger portions appear to be formed, but, in the latter, the component particles are not distinguishable in the same manner as the small rounded bodies above described, when they are collected together in groups. This infiltrated variety is not unfrequently primitive, according to Rokitansky, but, still more frequently, isolated tubercles pre-exist.

Colour.—Its colour is gray or yellow. When gray, it is semi-transparent, pearly, at times almost vitreous in appearance; when yellow, opaque. The shade of yellow is important. According to Lebert, it is never of an orange or ochre colour.

The gray and yellow colours are met with in both forms of tubercle, and sometimes the two are mingled, a gray granulation being perhaps yellow in the centre, or a large mass partly of one, partly of the other hue.

Consistence.—The consistence varies according to the stage in which the product is examined. We sometimes find near the firmer portions, a viscous synovia-like fluid, resembling in color the gray tubercle, of which, according to some, it is the earlier stage; Lebert, however, regards it as an exudation from which connective tissue is formed.

Gray tubercle is usually quite firm, elastic, difficult to subdivide with the dissecting needles, and when divided it breaks into fragments. Sometimes, however, it is soft and may be crushed into a continuous layer.

The yellow variety is softer, caseous, more brittle, and readily crushed.

Vascularity.—The question of vascularity has been so much discussed that it must be noticed here, although it is introducing among positive characters, what has no existence. Without referring to the statements made *pro* and *con*, it is sufficient to say that, where bloodvessels are found within a tubercular mass, they belong to the tissue in which it lies, and not to the tubercle, which is from its very nature non-vascular.

Microscopic Characters.—In endeavouring to ascertain whether there be in tubercular matter anything which the microscope can detect, we should if possible choose a part of the body, of which the natural elements are so simple as to furnish nothing which can simulate those of the new formation. Though all writers do not refer to this point there is sufficient correspondence between their observations to lead us to believe that proper precautions have been taken. Certain accidental products are, however, common to tubercle everywhere, and these we shall mention in their proper place.

The elements detected by the microscope are supposed to be common to both the gray and yellow varieties, and we will for the present accept this view, reserving for the future a more thorough examination of the question.

We must first make a distinction between the corpuscular elements and the substance which unites them.

The former may be subdivided into those belonging to the product when in a perfect state, and others probably resulting from some degenerative process or other change. Here, too, we are following the generally received opinion, with the intention of modifying it hereafter in conformity with our own views.

In the class first mentioned we have—

1. Minute molecules or granules, scattered in abundance throughout the mass, particularly in the yellow variety. All of these are not similarly affected by chemical reagents, the greater part remaining unchanged after the addition of the acids, alkalies, or ether. These have been regarded as modified protein compounds. We have, mingled with these, however, many fat globules.

2. Nuclei from 0.004 to 0.009 millimetres in diameter, either roundish or oval, usually containing in their interior some granules and a nucleolus.

3. Nuclei of various shapes without distinct nucleoli, and more or less defective, as is shown by their wrinkled irregular outlines.

4. Nucleated cells, according to Paget, misshapen, withered, and irregular, or, as Wedl states, sometimes elongated, and constituting merely the external layer of the new formation.

5. Compound cells of large size, and containing a number of nuclei.

6. The so-called tubercle corpuscles. Although these have a somewhat irregular angular outline, their form generally approaches the round or oval. A high power is necessary for their examination, as they are only from 0.005 mm. to 0.0075 mm. in diameter. A more or less transparent substance, and molecular granules fill the interior.

The above are the elements most commonly described in connection with tubercle. Although they may be accidental, it was thought advisable to separate them from those which are undoubtedly so, and which are—

1. Fragments of the various tissues involved in the disease.

2. Various products of inflammation, perhaps undergoing degeneration, such as pus-corpuscles, granular cells, or masses, etc.

3. Fat; sometimes in the form of vesicles, sometimes as granules of elaine or stearine.

4. Cholesterine, which, according to Lebert, is found only in cretaceous tubercle.

5. Calcareous granules found in the cretaceous tubercle, composed of the phosphate and carbonate of lime. These sometimes form shapeless masses.

6. Prismatic crystals, which are, however, very rare.

7. Pigment, which is met with in three forms according to Lebert; in grains, as spots, and as spherical melanic globules filled with black granules. This pigment, as the same author states, has never been found in the interior of the so-called tubercle-corpuscles.

8. Concentric colloid corpuscles are mentioned by Wedl.

We must now consider the interglobular substance, which unites the elements above described. This is pretty firm and semi-transparent, but presents no filamentous appearance. It is most abundant in the gray variety, and is more or less filled with molecules in the yellow.

Chemical Characters.—When we consider the difficulty of separating the tubercular matter from the tissues in which it lies, it will easily be understood that the results of a chemical investigation cannot be very satisfactory. Nothing peculiar to, or which throws any light upon the nature of the disease has yet been discovered. It is hardly worth while, therefore, to copy analyses, which would be useless in our present inquiry, since they are always accessible to those interested in them.

Metamorphoses.—Tubercle being unorganized and non-vascular, we might suppose that though capable of exciting changes in the parts in which it lies, it would undergo none itself. This, however, is not the case; it is exposed to a variety of metamorphoses, partly owing to the influence of the living tissues, partly to physical changes within itself.

In the first place, the gray may be transformed into the yellow. Although the infiltrated variety undergoes this change, it may be best observed in the discreet granulations, in which the centre first becomes opaque. This, as we shall hereafter see, is precisely what might be expected, the deeper seated parts being the oldest.

Gray tubercles in the lungs are also subject to a peculiar change, in which they lose their lustre, become dry, hard, horny, and shrivel into shapeless masses. This indicates that the substance is no longer susceptible of change.

The yellow and mixed forms may gradually become cretaceous. This, like the previous change, is curative. A mass which is undergoing this transformation becomes more consistent although the cohesion may be less; it is whiter, gritty to the feel, and when pressed between two slips of glass resists much more than before. At a later period, it resembles plaster or lime with which a little water is mingled. Finally, a concretion of stony hardness may be formed, sometimes of considerable size, though rarely larger than a pea.

At the commencement of the change the interglobular substance presents, in addition to the ordinary molecules, mineral particles which are detected rather by their resistance to compression than by any other peculiarities. These particles gradually increase until the substance is occupied by them. In addition to the above, crystals of cholesterine are found, and the dark pigment previously described. This cretaceous change has been most frequently noticed in the lungs and bronchial glands.

Yellow tubercle may also soften. This change may commence in the centre, at the periphery, or in both places at once. In the tubercular matter itself, it is never a vital process, and may take place independently of inflammation or exudation from the surrounding tissues. Though morbid secretions may aid somewhat in the disintegration of tubercle, they are not essential to it. It is a purely physical change, dependent upon the absence of nutrition, and is therefore seen in the deeper-seated or oldest parts of the distinct nodules, even where these are of considerable size. At an early period, the softened portion looks more crumbling than the remainder, and is very easily separated from the firmer part, leaving a little cavity. At a later period it becomes liquid, like pus, with flakes or grumous masses floating in it. These last may be undissolved portions of tubercular matter. But this liquid is not pus, for, into this, tubercle is never transformed. When there is an admixture of pus globules, they must be derived from the adjacent tissues, for these alone possess the vascularity absolutely essential for the formation of a purulent fluid.

Although the friable grumous condition may precede liquefaction, it may exist a long time without the latter taking place, and be followed by the cretaceous change. Under the microscope, a mass which is softening presents different appearances according to the stage at which it is examined. At one period the so-called tubercle corpuscles will be distinctly seen, but they afterwards disappear, and we have nothing but an abundance of molecules, with particles of oily and calcareous matter.

The product thus formed is usually discharged, the surrounding tissues having ulcerated; but it may be retained. In this case the fluid parts are gradually absorbed, while the fatty and calcareous matters increase until it is converted into a dry, friable, mortar-like or hard concretion.

Changes in the adjacent Tissues.—Having considered the changes which take place in the tubercle itself, we will glance at those which affect the tissues in which it lies. Its presence may cause the destruction of the adjacent and included parts, or give rise to the formation of new tissue. The inflammation excited may be followed by the expulsion of the tubercular mass, either before softening has taken place or after. This may be a curative process, but also one attended by danger, and, though all the tubercular matter be expelled, there is a constant tendency to the formation of more in the walls of cavities, and in the basis and borders of ulcers. In the same parts new cellular tissue may also be formed, and this may finally become tubercular. The melanotic condition so often seen probably has its origin in the transformation of hæmatin, and is perhaps preceded by the obliteration of vessels, whose contents afterwards become changed.

Parts affected.—Not only almost every organ and tissue may be the seat of tubercular disease, but new formations, such as cellular tissue in cicatrices, and in the borders and bases of ulcers. Though showing a decided predilection for some organs more than others, its tendency is to invade one part after another, or several simultaneously. This disposition to generalization is particularly marked in infancy.

Notwithstanding the various opinions advanced with regard to the exact seat of tubercle, it seems quite evident that it is deposited particularly in the cellular tissue of organs, among the elements of which they are composed, as between the bronchi and vessels of the lungs, between the nerve-tubes, or between the tubuli or other elements of the secreting organs. It is also seen on the surface of membranes, as in the genito-urinary organs, the bronchial vesicles or minute bronchi.

Frequency in different Organs.—It is impossible to settle summarily the question of frequency in different organs. No single table will suffice. We may, it is true, state absolutely that some organs are particularly exposed to the attacks of this disease, while others are almost exempt. But, with regard to the former, the liability varies at different periods of life and according to the primary or secondary character of the affection. With regard to the latter we may be more absolute, as there are some parts which are scarcely ever affected, such are the salivary glands, the ovaries, the walls of the bloodvessels, the œsophagus and vagina.

The statements of different authors, concerning the relative frequency in organs, do not agree, and being based upon facts, are of course irreconcilable. We shall therefore be justified in adopting the opinion of one like Rokitansky, who has had the largest experience and the best opportunity for judging. According to him, the scale is somewhat as follows: the lungs, the intestinal canal, the lymphatic glands (particularly the jugular, the bronchial and abdominal), the larynx, the serous membranes, pia mater, brain, spleen, kidneys, liver, bones, and periosteum, uterus and tubes, testicles with the prostate and vesiculæ seminales, spinal cord.

In children, on the contrary, the lymphatic glandular system holds the first place with the spleen, afterwards the lungs with the bronchial mucous membrane, then the brain, serous membranes, etc.

In estimating its frequency as a primary or secondary lesion, we arrive at still different results. Though the lungs and lymphatic glands still hold the same position, the scale in other respects may be entirely changed. Thus, the urinary organs, the female sexual mucous membrane, the bones, the testicles, the prostate and vesiculæ seminales, which stood at the bottom of the list, follow closely the organs first mentioned; while the intestines, larynx, trachea, serous membranes, spleen, and liver, are almost never the primitive seat of the disease.

In addition to the above peculiarities, certain organs are likely to be affected simultaneously, or nearly so.

The disease not only shows a disposition to invade certain organs, but certain parts of those organs, as the apices of the lungs, that portion of the pia mater which lies at the base of the brain, the gray substance of the brain itself, the spongy bones and spongy portions of the long bones, the lower part of the small intestine, the fundus of the uterus, &c. But, in the midst of this almost universality of invasion and destruction we see certain limits to its power. From the larynx, it almost never extends to the pharynx, or from the fundus of the uterus, through the internal orifice.

Incompatible Diseases.—Fortunately, also, there are conditions of the body, with which it seems to be nearly or quite incompatible. These, according to Rokitansky, are—

1. Cancer, which is extremely rare in connection with tubercle.

2. Typhus. (By this is probably meant our typhoid.) This is decidedly exceptional in tubercular individuals.

3. Rickets is not often seen in connection with it, and the combination of the two is especially rare, when deformity has resulted from the disease of the bones, and the chest has become narrow.

4. Derangements arising from mechanical obstruction of the circulation in the heart and lungs. Under this head we may class the following conditions:—

a. Obstructions at the orifices of the heart and consecutive enlargement of the latter.

b. Congenital malformations of the heart and the arterial trunks, such as absence, narrowness, persistence of the thoracic duct.

c. Many acquired anomalies of the arterial trunks, resembling congenital arrests of development, such as those resulting from compression; also dilatations, as aneurism, particularly when in the neighbourhood of the heart.

d. Diminution of the capacity of the thoracic cavity, caused either by a great degree of deviation of the vertebral column, by advanced pregnancy, or by large ovarian cysts.

e. The original small size of the pleural sac and lungs.

f. An enlarged thyroid gland, chronic catarrh, dilatation of the bronchi, or pulmonary emphysema.

There are, of course, other facts which might be alluded to in the general history of tubercle, but it is believed that the above are the most important in connection with the inquiry we are about to make, and more perhaps than we shall use.

Assuming, then, that they represent fairly the present opinion concerning the anatomical characters of the new formation, we have yet to decide upon their relation to, and the real nature of the latter. For this purpose we must make use of the clinical history of cases as well as of the unaided eye, the microscope and other means, which can throw light upon the physical characters of the affection.

Our inquiry should be directed to three points, within which appear to be comprised the questions which may arise.

1. Is tubercle a "specific exudation poured out under the influence of a special, general pathological state?"

2. Is it a degraded condition of the nutritive material from which the textures are formed, differing from that furnished under ordinary circumstances not in kind but in degree of vitality or capacity for organization?

3. Is it the result of the metamorphosis of elements normal or pathological?

Within the last few years we have met with a variety of cases which seem to throw some light upon the above points. In the greater part of them the statements are mostly confined to the anatomical and microscopical characters, either because the nature of the disease was undoubted and too well understood to render it necessary to give more than its name, or because the clinical history did not appear to have any bearing upon the present investigation.

It will also be noticed that in the microscopic examinations no allusion is made to any of the elements described, except the so-called tubercle-corpuscle. This is the only one about which there is any dispute. The others, certainly, are not peculiar to tubercle, although so frequently found in it.

Cases.—In a large number of cases in which both the gray and yellow varieties were examined microscopically, the so-called tubercle-corpuscle was found. There can, therefore, be no doubt about the existence of this—that it is almost universal in formations which are considered tubercular. But we must look still farther and endeavour to ascertain whether it be not also found elsewhere, and under what circumstances it is wanting.

CASE 1. *Infiltrated tubercle: absence of any peculiar elements.*—In Jan., 1857, a child was examined, who died with well marked tubercular formations in various organs. In the lungs were cavities, yellow caseous matter, and a large amount of grayish-white material. The latter, examined with the microscope, was found to contain *nothing but epithelium cells.* It seemed to be characterized rather by the absence of peculiar elements than by anything else.

CASE 2. *Miliary granulations containing hardly a trace of the peculiar corpuscles.*—In 1852 a case was examined, in which very firm miliary granulations were found in the lungs. One of these proved to be so firm that it was with difficulty subdivided by the dissecting needles. Under the microscope, much cellular tissue was noticed and many epithelium cells; but also a very few suspicious looking bodies, "which resembled in some respects the tubercle-corpuscles."

CASE 3. *Gray granulations containing altered epithelium and tubercle-corpuscles.*—In a person who died of acute phthisis, the lungs were found crowded with gray granulations, softer than those above mentioned. They contained, besides "tubercle-corpuscles," *large cells filled with fat globules and granular matter. These were probably epithelium cells* *which had degenerated.* (Fig. 1.) In the apparently healthy intervening portions of lung, the same elements were seen, and also cells in which the nucleus was still visible. The pulmonary tissue was also infiltrated with fat. (Fig. 2.)

Fig. 1.

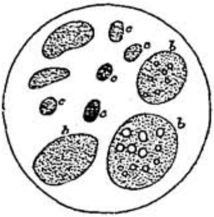


Fig. 2.

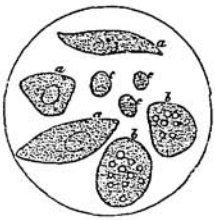


Fig. 3.

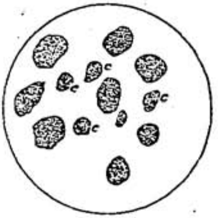
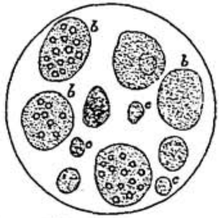


Fig. 4.



a. Epithelium. *b.* Degenerated epithelium. *c.* "Tubercle corpuscle."

The above appearances were compared with those presented by yellow caseous material taken from a patient who died of chronic tubercular disease. In this, granular corpuscles of various sizes were seen, but none as large as those spoken of above as epithelium. Many were of the size, and resembled in every respect the "tubercle-corpuscle." (Fig. 3.) In the intervening portion of lung, however, the same large degenerated cells were found as in the other specimens. (Fig. 4.)

CASE 4. *Degeneration of epithelium in connection with tubercular disease of the lungs.*—In a case examined in Dec. 1857, the lungs were found crowded with tubercles. Some parts in which no decided deposit had taken place, had a yellowish tinge, and, under the microscope were seen to contain many large cells filled with minute globules; evidently epithelium undergoing fatty degeneration.

CASE 5. *Same change as in the above.*—In the lungs of a person who died in April, 1858, there was found very extensive tubercular disease, partly in the infiltrated form. On examining the more dense red portions between the deposits and the parts containing the fine tubercular dust, there were seen many large corpuscles filled with minute globules; others of the same size containing nuclei partially obscured by the contents; and many much smaller, down to the so-called tubercle-corpuscle.

CASE 6. *Same change. Resemblance of the nuclei of the epithelium to the "tubercle-corpuscles."*—In Oct. 1858 a woman died suddenly of pulmonary hemorrhage. In the lungs was a small amount of yellow tubercle and some gray, the latter in the form of an infiltration. In the last were many perfect epithelium cells and some tubercle-corpuscles, but these resembled the nuclei of the first. In some parts which had a yellowish tinge the epithelium cells had become quite granular or had disappeared, while the tubercle-corpuscles were much more abundant.

CASE 7. *Pneumonia: fatty degeneration of the epithelium.*—A man died after being sick a fortnight with the usual symptoms of pneumonia. Nearly the whole of the right lung, from the apex downward, was hepatized, and much of it in the third stage. On examining portions which were still elastic, though probably somewhat diseased, the epithelium cells, or others of the same size, were found opaque, granular, and partially or entirely filled with fat globules. There were also many small opaque corpuscles. In parts which had reached the third stage, there were many pus globules, with here and there a large cell like those above described.

CASE 8. *"Yellow infiltrated tubercle." Fatty degeneration of the epithelium. "Tubercle-corpuscles" resembling the nuclei of the epithelium.*—In Sept. 1858 a man, after exposure to cold, was attacked with cough, dyspnœa, and other thoracic symptoms of a subacute character. For some time he was able to keep about, and several weeks after entered the hospital. The physical signs were such as are usually found in connection with consolidation of the lung. The sputa, however, were not peculiar, and the symptoms never resembled those of ordinary acute pneumonia. He steadily failed, and died four months after the commencement of the disease. At the examination, there was found scattered throughout the left lung, from apex to base, a dull yellow material in the form of small points or large irregular masses, the last evidently resulting from the aggregation of the first. The lower lobe was for the most part occupied by this adventitious product. In the upper lobe was a cavity filled with dirty pus. The other lung was similarly affected, but less extensively. Near the confines of the disease were several reddish, firm portions of small size, resembling the pulmonary tissue in a state of red hepatization. On examining the last with the microscope there were seen epithelium cells, in some of which nuclei were still visible. There were also other cells of the same size filled with minute globules or granules; and mingled with these many others of various sizes down to the "tubercle-corpuscle." The latter resembled in every respect the nuclei of the epithelium.

In the more abundant yellow material at the base of the left lung there were seen the same "tubercle-corpuscles" and the same large cells filled with minute globules, but very little, if any, healthy epithelium. The bronchial glands contained a little caseous or cretaceous matter. In the lower part of the small intestine were a few small ulcers and a little yellow material. The mesenteric glands were enlarged, and contained a yellow tubercular deposit.

CASE 9. *"Yellow infiltrated tubercle." Fatty degeneration of the epithelium.*—A young man, 17 years of age, after wetting his feet, was attacked with cough and other thoracic symptoms, not sufficiently severe, at first, to confine him to his bed. He raised a little blood several times, and, his health declining, finally entered the hospital, after which the sputa were several times reported as rusty. The symptoms, however, were more those of phthisis than of pneumonia, and the physical signs did not point particularly to the latter. He died after an illness of about ten weeks.

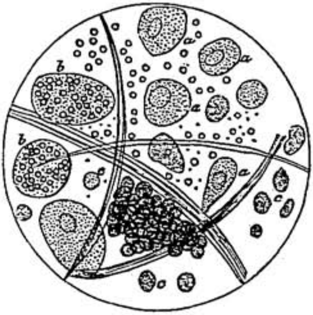
Much of the right lung was occupied by large yellowish-white masses, closely resembling infiltrated tubercle. The other organs were not examined, but there was no reason to suspect disease in any of them. The microscopic characters were, on the whole, the same as those described in previous cases, viz., epithelium more or less degenerated, and corpuscles of various sizes, down to the tubercle-corpuscle.

In connection with the last two cases, it may be well to allude to those published by Dr. Bowditch in the *American Medical Monthly* for July, 1855, entitled—

"*Cases of anomalous development of tubercle, commencing at the base of the lung and gradually extending upwards; with the physical signs of pneumonia.*"—In several which were examined after death the appearances were such as have always been regarded as belonging to tubercle. In one in which the microscope was used the results were as follows:—

"To the naked eye the tubercular deposit was present in three distinct forms: 1st, as isolated, round, yellowish-white granulations, about a line in diameter, and separated from each other by pale red pulmonary substance; 2d, as a yellowish-white, almost diffluent or gelatinous matter, a small quantity of which only was seen; 3d, as a yellowish granular substance, containing but little moisture. This last form was most abundant, occupying, in large irregular masses, the pulmonary tissue. On microscopic examination, the first two varieties were found to contain essentially the same elements as represented in Fig. 5, viz., epithelium, 'inflammation corpuscles,' and

Fig. 5.

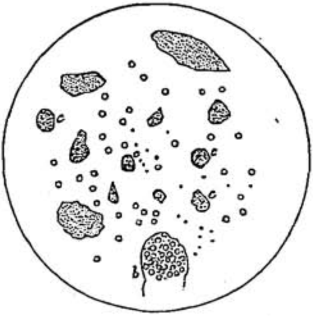


a. Epithelium. *b.* "Inflammation-corpuscles." *c.* "Tubercle-corpuscles."

others of various sizes (the latter unaffected by acetic acid), forming a regular series down to the so-called tubercle-corpuscle. In addition to the well-marked epithelium cell, others were seen in which the nucleus was almost obscured by the minute globules, which entirely filled, and gave the peculiar character to, the 'inflammation corpuscle.'

"The appearances in the third variety are represented in Fig. 6. Here the larger corpuscles had almost entirely disappeared, a few fragments only remaining, while the number of so-called tubercle-corpuscles had much increased. Numerous minute globules and granules were floating about in all the specimens."

Fig. 6.



b. "Inflammation-corpuscles." *c.* "Tubercle-corpuscles."

CASE 10. *Cancer, containing well-marked "tubercle-corpuscles."*—In a breast removed at the hospital by Dr. Cabot in March, 1859, the appearances were those of ordinary scirrhus, and there were none of the usual signs of degeneration. It was found to be composed of fibroid tissue and corpuscles of various sizes, none very large, and many so small and granular as to resemble precisely, when examined with a high power, the so-called tubercle-corpuscle.

CASE 11. *Cancer presenting the usual appearances of tubercle, attributable to the fatty degeneration of the cells.*—It is so common to find yellow "phymatoid" material in growths unquestionably cancerous, that we do not consider it necessary to cite any single case, but make the general statement that in a large number of instances we have found the change owing to the fatty degeneration of the cells, which may still retain the form of the more healthy ones among which they lie.

CASE 12. *Caries of the spine. Cavities in the bone filled with a yellow caseous substance, which extended downwards along the spine and psoas muscle to the thigh.*—In this case the bodies of the three last lumbar vertebræ and the upper half of the sacrum were extensively carious. Deep cavities in the former were filled with a yellow, soft caseous substance like soft tubercle or inspissated pus. Those portions which still retained their usual form were infiltrated with a thick red fluid. A caseous material like that described above filled a cavity between the diseased bones and tissues around, and extended downwards in the substance of each psoas muscle, on the left side as far as Poupart's ligament, and on the right, apparently as low as the thigh. The substance within the muscle was considerably drier than that in the neighbourhood of the bone.

Taking into consideration the disease of the bone and the course pursued by the caseous material, there can be no doubt that the latter was merely inspissated pus, and yet it is precisely like what Nelaton describes as tubercle in connection with tubercular disease of bones.

CASE 13. *A formation apparently tubercular in the diaphragm. Nothing peculiar noticed with the microscope.*—In a patient who died of tubercular disease of various organs, there was also seen beneath the serous membrane covering the diaphragm a yellow deposit resembling those found elsewhere. Unlike them, however, it contained no peculiar corpuscles, but merely irregular masses and small fragments.

CASE 14. *A formation apparently tubercular in a supra-renal capsule. Nothing peculiar noticed with the microscope.*—In the supra-renal capsules of a patient who died without manifesting any decided symptoms except debility, yellow deposits were found resembling very closely yellow tubercle, but, on microscopic examination, nothing was seen but an amorphous mass.

CASE 15. *Disease of the kidney simulating tubercle.*—A sacculated kidney, in which the sacculi were evidently dilated calices, was filled with a soft substance like thin mortar, which might be mistaken for tubercle. This, on microscopic examination, proved to be composed of minute globules and irregular granular corpuscles, some like those so commonly found in tubercle, but many much larger. The material was undoubtedly inspissated pus, as there was ulceration of the bladder, and the patient had had urinary symptoms for four or five years.

CASE 16. *Fibroid and fatty degeneration of the placenta, resembling yellow tubercle.*—A case of this kind is reported in the *Transactions* of the Boston Society for Medical Improvement (vol. ii. p. 292). In the substance of the placenta were a number of firm yellowish-white masses, some of which closely resembled tubercle. These were found to be non-vascular, and the villosities, where seen, had a more or less fibroid appearance, and contained granular matter or minute fat globules. This is not an uncommon appearance, and has been described as "tubercular degeneration."

With these cases before us, let us see if we can draw any conclusion concerning the anatomical character of tubercle, or the relation of the latter to other morbid processes.

Examining, in the first place, the appearances which the naked eye can appreciate, can we trust to them as evidence of the nature of the product? Let us first take into consideration the yellow variety, as this is the most common and the one about which there probably prevails the largest amount of error.

We have seen this yellow material mingled with the semi-transparent, also in cases which, judged clinically or anatomically, might leave us in doubt about their pneumonic or tubercular character; in cancer (Case 11); in caries of the spine (Case 12); in the supra-renal capsule (Case 14); in the pelvis of the kidney (Case 15); and in the placenta (Case 16). As far as the unaided eye can teach us, this peculiar appearance belongs to a great variety of products.

On pushing our inquiry still farther with the aid of the microscope, we find that in the lungs the epithelium becomes fatty and is gradually destroyed, that the same change takes place in the cells of cancer and in the villous structure of the placenta; that in the spine and kidney the products of inflammation have evidently undergone a change; that in the supra-renal capsule there is nothing which would indicate the original character of the disease. With nearly the same external characters, these formations present very different appearances when examined with the microscope, *but they have one property in common; they show the most undoubted signs of degeneration.*

But this does not settle the question. Do they not contain, in addition, some elements which will enable us to distinguish one from the other? Now the only one which has been considered at all peculiar to tubercle is the small granular corpuscle. As we have seen, that exists in a large number of cases, but even in those, about the nature of which there could hardly be a dispute, it is found in such a connection that we are led to believe that it is only a shrivelled cell or free nucleus. But its existence in cancer (Case 11), in products evidently inflammatory, etc., furnishes us with still stronger evidence of its non-specific character.

We must, therefore, conclude that this material is simply the result of degeneration, and not necessarily indicative of any special disease.

But the conclusion implies that something existed which could degenerate. Can we not still then find a product, which we may call tubercle, possessing this tendency to decay in common with other new formations. Now, if there be anything anterior to the yellow variety, it is the gray, and to this we necessarily turn.

We have seen that it may be converted into the yellow (in other words, may degenerate), and therefore have reason to believe that some of the elements (such as tubercle corpuscles) found in it belong to the latter (yellow), and they appear to increase as the colour changes and deepens (Cases 1, 2, and 3). In Case 1 the infiltrated gelatinous material contained nothing which could be considered at all characteristic, and the same substance in Case 6 was almost as free from peculiar elements, which were also almost entirely wanting in Case 2.

May we not, therefore, conclude that gray tubercle, at an early period, possesses no anatomical element, which will enable us to distinguish it from other morbid products?

Must we, therefore, deny the existence of such a new formation as tubercle? Not at all. We only deny that it has any special structure.

The peculiarity of the product is *its tendency*, of which we have numerous instances every day. This we cannot understand any more than we can the property of the syphilitic virus, which produces such a variety of changes in the human body. Yet no one doubts its specific power. (This is used merely as an illustration.)

We are certainly left with rather a vague principle with which to work out the great question, the decision of which is the chief object of the essay, and it appears all the more difficult to solve, when we consider that inflammation itself is a very vague and but partially understood process.

Still, accepting the term in its usual sense, we may again refer to our cases.

In No. 7, which was one of genuine pneumonia, the degeneration of the epithelium was quite as marked as in any of those which were decidedly tubercular. Pus corpuscles were also found.

In the next case, No. 8, we have a formation a little older; one which would certainly be called infiltrated tubercle. Here the same degenerated cells were found and others of various sizes, down to the "tubercle-corpuscles," which resembled the nuclei of the epithelium, increasing as before in proportion to the amount of the yellow material.

The cases reported by Dr. Bowditch are very valuable in this connection. Commencing with the physical signs of pneumonia, they pursued a subacute or chronic course until they terminated in death. The lungs, in those examined, were occupied by what were considered well-marked tubercular formations. In the one which was examined microscopically some of the changes noticed were precisely the same as those belonging to acute pneumonia, and the other appearances were such as we might expect to result from the progressive degeneration in the older product.

It appears, therefore, that the relation between the yellow material and inflammation is very intimate; that the so-called tubercle is merely the result of the degeneration of the inflammatory product and the elements of the tissues in which it lies.

Taking this view, we must conclude that the cases reported by Dr. Bowditch, and others resembling them, originated in inflammation.

But it does not follow that products like those described are always preceded by inflammation. The connection between the two, though frequent, is accidental, as we have shown by a number of cases. The great mistake in attempting to decide the question, has been that of basing the conclusions upon the degenerate formation.

The appearances noticed in a number of specimens of pneumonic lungs, examined with the microscope, seem to explain, to a certain extent, how the peculiar change of colour and consistence may take place in inflammation. On examining portions of pulmonary tissue, which appeared to be but slightly affected, and which still retained much of the red colour, we found, contrary to what was to have been expected, according to the description usually given, a decided diminution or absence of red globules, while the tissue was filled with many small granular corpuscles, closely resembling those of pus or the white blood-corpuscles. If the absence of blood continues, and the corpuscles described remain or increase, the pulmonary substance must degenerate and become dry, or soften. In the first case, we should have precisely the appearances seen in what is called yellow infiltrated tubercle, without the acute symptoms which attend the rapid formation of the pus, as in the third stage of pneumonia, when softening takes place.

We have now to discuss the question of the relation between the gray variety of tubercle and inflammation. The inquiry here must necessarily be more or less of a speculative character. We have no anatomical elements to compare, for we have declared our belief that the peculiarity of tubercle is its tendency. Now it is possible that as exudations are often the result of inflammation, their character may be so influenced by general or local causes that "tubercle" is the consequence, when it might never have been developed under ordinary circumstances. Examining the question clinically, we can come to no more positive decision. Tubercle makes its appearance sometimes with, sometimes without symptoms of inflammation, and, certainly, the recent granulations, in most cases, show no signs of an inflammatory origin: the tissue in their neighbourhood is remarkably healthy. If therefore they generally or often exist without apparent inflammation, the presence of the latter should rather be regarded as a consequence and not a cause.

Although the questions proposed at the commencement of the inquiry have been sufficiently answered, it may be well to briefly state our conclusions here.

It is not a specific exudation. It does not exist, as such, in the blood.

The yellow variety is always the result of metamorphosis—of degeneration.

It is altogether probable that it is owing to a "degraded condition of the nutritive material," which differs from that furnished under ordinary circumstances, "not in kind, but in degree of vitality or capacity for organization."

The descriptions usually given of the anatomical characters of tubercle are for the most part correct, but the real nature of the disease has been almost universally misunderstood, and the term applied to lesions of an entirely different character. All circumstances must be taken into consideration in forming an opinion about such cases.

These results are based upon observations of our own, made before we became aware of the fact that they only confirmed what was announced long ago, and quite well demonstrated too. In 1692 a dissertation was published by Zwilling, "De natura et cura phthiseos." In this he asserts that "Quicquid potest causari pulmonum inflammationem, potest etiam causari phthisin." Many men of note have since taken the same ground; but with the means which they possessed for the investigation of the subject, their views could not be so satisfactorily proved as those of the writers of the present time.

To the last, therefore, we shall appeal for the corroboration of our own statements.

The writings of Rokitansky, Paget, and Wedl, show that gray tubercle may undoubtedly be converted into yellow, though the change is sometimes so rapid, as to give rise to the idea that the formation is originally yellow. Even Lebert admits that when it takes place, the number of "tubercle corpuscles" increases. This metamorphosis, however, is like that seen in the elements of tissues and adventitious growths, which have no connection with gray tubercle. It occurs in such as are composed of nuclei and nucleated cells; in cancer, in the elements of exudations, in pus, and in the material met with in some cases of typhoid fever. Formations in the bones, cellular and adipose tissues have also been mistaken for it.

Paget states that—

> "It is common to find in medullary cancers, and. more rarely in others, portions of yellow, half dry, crumbling and cheesy substance, so like tubercle that with the naked eye, they can hardly be distinguished from it. The cancers in which they occur have been described as mixtures of cancerous and tuberculous

matters; but the microscope finds that the tuberculoid, or, as M. Lebert calls it, the phymatoid material in them, consists of cancer corpuscles, withered, with fatty and calcareous degeneration, and mingled with molecular and granular matter. By similar degeneration, material like tubercles may be found in cartilaginous, rudimental, fibro-cellular, and probably other tumours. In all these instances the microscope may usually insure a just diagnosis, and may prove that the tuberculous appearance is only due to a withering and fatty degeneration of materials, that have nothing but their degeneration in common with true tuberculous matter."

Having thus confirmed our former statement, that yellow tubercle is a degenerated product, we may now take into consideration the character of the other variety.

Virchow (*Gesammelte Abhandlungen*, p. 216) states that—

> "Young gray tubercles resemble so closely the material which forms the follicles of the cortical layer of the lymphatic glands, that they may be mistaken for it, and, certainly no greater correspondence can be found than that which exists between the follicles of the spleen and the small interparietal tubercles of the bloodvessels of the brain in tubercular arachnitis."

As no mention is made of the microscope, the above remarks probably refer to the appearances of such bodies when examined with the naked eye. If so he might also have alluded to the small fibroid granulations sometimes met with in serous membranes.

With regard to the gray gelatinous material, Reinhardt (*Annalen des Charité—Krankenhauses.* Berlin, 1850) describes it as a clear, transparent and somewhat viscous fluid, resembling in consistence a moderately concentrated solution of albumen. Under the microscope it appears completely homogeneous and transparent, but sometimes contains epithelium cells enlarged and infiltrated with fat, and also pus-corpuscles from the bronchi.

The gray granulations, he seems to think, are composed of the same material, which may form cellular tissue. This is certainly in opposition to the opinion of Rokitansky, who declares, that if adventitious growths resembling tubercle in external form and original composition show a fibrous structure, they cannot be tubercle.

The view taken by us of the nature of the latter seems to explain these differences sufficiently well. A fluid may exist, apparently homogeneous; but a part of it, however, possesses sufficient vitality to form cellular tissue; the remainder may become what is called tubercle, may present no definite structure, and show a marked tendency to degenerate.

As our conclusions with regard to gray tubercle seem to be also sustained, we will now consider the relation of the new formation to inflammation. As the views of Virchow and Reinhardt include those which have been advanced by other writers, we cannot do better than to give an abstract of them.

We will commence with a description by Reinhardt (*Annalen, etc.*) of a class of cases resembling in a most remarkable manner several reported by us.

> "We see in persons previously healthy, and not predisposed to tubercular disease, cases of inflammation of the lungs, which are usually the result of great exposure to the cold. They begin with fever, pain in the side, dyspnœa, the expectoration of bloody sputa, and the physical signs of infiltration of a large portion of a lung. In a word, they resemble those of ordinary acute lobar pneumonia, but differ from the latter in their farther course. After the subsidence of the

fever and other rational symptoms, there is no absorption, no resolution of the exudation; the affected portion of the lung remains impermeable to the air. After the disappearance of the rational symptoms in such cases, the patients may regain their health, although the exudation in the lungs is not absorbed; but more frequently, particularly where the infiltration is very extensive the health is not entirely regained, and the case finally terminates fatally. Such cases have been regarded as chronic pneumonia.

"On examination we find no traces of previous tuberculosis. Where inflammation has been excited anew a short time before death, we find the part most recently affected, voluminous, without air, not granular, and of a whitish-gray colour, perhaps bordering upon red. The infiltrated pulmonary tissue, although its elasticity is diminished, is not as friable as in ordinary pneumonia. On pressure there escapes a clear, transparent, somewhat viscid fluid, resembling in consistence a moderately concentrated solution of albumen. This, under the microscope, appears completely homogeneous and transparent, though it sometimes contains *epithelium cells enlarged and infiltrated with fat*, also pus-corpuscles from the bronchi.

"After the disease has lasted several weeks we find the external surface of the lung either smooth or depressed at certain points. The cut surface is smooth and of a gray colour, and presents a varigated appearance, owing to the existence of two distinct products; one, yellow or yellowish-white, is composed of the enlarged and fatty epithelium cells; the other, which is whitish or grayish-white, results from the increase or thickening of the interstitial tissue. The exudation pressed from the affected part appears somewhat thicker and more opaque than in the earlier stage. With the microscope we recognize the usual forms of *degenerating epithelium*, the cells being enlarged and more or less filled with fat and large protein-granules. A part have smooth outlines and distinct nuclei, while others want the latter and are shrunken. We also have irregular fragments as well as fat and protein-molecules, resulting from the destruction of the above-mentioned elements.

"At a later period the lung may shrink still more and be converted into a solid, gray, or blackish-gray mass, composed of cellular tissue and bloodvessels, and finally, when the vascularity diminishes, be transformed into a firm cicatrix-like substance."

But cases do not always terminate in this way. Spiess (*Pathologische Physiologie*, p. 423) states that "the exudation which has become hard, and more or less dry and shrunken, may undergo further changes, may be decomposed like the original inflammatory products and give rise to materials which may excite inflammation in the organs, perhaps of a slow and destructive kind."

Isolated tubercles Reinhardt thinks are formed in the same way as the more extensive infiltration; the change, however, is confined to limited portions of the lungs.

He speaks also of a form in which the affected part is the seat of gelatinous infiltration and yellow points surrounded by it, the whole having the appearance of tubercular infiltration composed of gray and yellow material. In a case which had lasted three weeks, he found in the midst of the gelatinous substance numerous small yellow points which proved to be pus, and he traced this through various changes down to the yellow tubercle. The pus became thicker and thicker, while the globules lost their regularity of outline and were less affected by reagents. At the same time the nuclei became indistinct and finally disappeared, so that the cell was transformed into a solid homogeneous mass, precisely resembling the so-called tubercle corpuscle.

The above remarks refer to chronic pneumonia, but precisely the same changes were noticed in cases which would undoubtedly be considered tubercular.

The same transformation of pus into a yellow caseous substance is seen in the liver, testicles, kidneys, &c. In the mucous membranes, tubercle corresponds with dried purulent formations; also, sometimes, with an amorphous diphtheritic exudation. Ulcers result from the separation of the parts thus affected, or they may originate in follicular abscesses, or in the usual manner. The caseous masses, the so-called free tubercle on mucous surfaces, as in the bronchi, the Fallopian tubes, the vas deferens, the vesiculæ seminales, etc., are only thickened purulent secretions of the mucous membrane.

[This last we consider altogether too sweeping a statement. Undoubtedly much and in many cases, the whole of the formations in those parts which are regarded as tubercle, result entirely from changes in the products of inflammation, but it does not follow that they may not originate in some other way.]

The connection between tubercle and inflammation is also seen in the serous membranes. At an early stage of the disease in tuberculous individuals, we find the synovial membrane crowded with blood, swollen, and infiltrated with a serous, gelatinous, or purulent exudation. Sometimes small abscesses are seen in the membrane. The cavity of the joint is filled with a sero-purulent or purulent fluid. We also meet with large masses of fibrin, containing more or less pus. When the inflammation subsides, the pus and amorphous fibrin degenerate and form yellow tubercular matter. These changes may be observed where the inflammation is owing to mechanical causes, such as wounds, fractures, etc. If such a joint be examined some time after the inflammation has subsided, we find the same appearances as in tubercular affection of the part; small granulations in the synovial membrane; the infiltration of the same with yellow caseous material, and finally deposits of a yellow tuberculoid substance in the cavity.

Virchow (*Verhandlungen der Physicalisch-Medicinischen Gesellschaft in Würzburg*, vol. i.), in speaking of what he calls tuberculous inflammation, states that—

> "We may in many cases convince ourselves that cellular tissue and tubercle make their appearance on serous membranes, in the same layer, which must be regarded as an exudation, originally consisting of coagulated fibrin. The question now arises whether the tubercle has arisen from this coagulum, that is, from the inflammatory exudation? Rokitansky has assumed that the elements of the two are originally mingled. But nothing of the kind can be demonstrated. It is much more reasonable to suppose, that while one part is transformed into cellular tissue, nuclei and cells form in the other. Then degeneration begins; after a partial fatty metamorphosis the cells decay, leaving behind a granular detritus, in which the nuclei are still, for some time, to be seen as shrunken, irregular, opaque bodies, which finally also decay, and nothing remains but an amorphous granular mass."

This still seems to confirm our own views, whatever the intention of the writer may have been. We have assumed that the marked characteristic of tubercle is its want of vitality. In the exudation above mentioned, a part is converted into cellular tissue. In the remainder, are formed feeble cells, which soon degenerate. At the commencement, the material from which both were formed appeared homogeneous, but a part only would admit of organization; the remainder made a feeble effort in the same direction and degenerated.

Reinhardt, after insisting thus strongly upon the connection between tubercle and inflammation, asks whether a general disorder, at all events a disease of the nutritious materials, does not lie at the bottom of the contemporaneous appearance in various organs of the tuberculous material? The answer is in the affirmative.

> "When we see," he says, "how children of phthisical parents, although brought up with the greatest care, and guarded from injurious external influences, are attacked by tubercular arachnitis, or at a later period, by pulmonary tuberculosis, we cannot possibly doubt the existence of a hereditary general disorder upon which the local affections depend. But, in cases of acquired tuberculosis also we have often an opportunity to see how the local affection is preceded by general derangement, loss of appetite, languor, and debility. In acute tuberculosis this general disorder assumes even the character of typhoid fever. Still farther, the influences under which tuberculosis is developed, such as bad nourishment, impure air, want of exercise, etc., are precisely those which are followed by derangement of nutrition."

Reinhardt throughout is labouring to prove that the relation between tubercular disease and inflammation is a very intimate one, and he *does* prove it. He, however, overlooks one very important point: that they are not necessarily connected. We cannot close this essay more appropriately than by giving a summary of Virchow's views (*Verhandlungen*, etc., vol. ii.), as they include most of the important points upon which we have insisted. They seem, however, to refer particularly to the yellow material.

> "1. Tuberculization, the undoubtedly local process by which is formed the product known as tubercle, does not consist in a peculiar specific exudation, *but in a peculiar transformation of the elements of tissues*, which, in 1847, I described in cancer under the name of tuberculoid metamorphosis.
>
> 2. The tuberculoid metamorphosis is coördinate with the fatty, waxy, cretaceous and atheromatous change, but not at all with inflammation, dropsy, suppuration, or the formation of cancer. [This is the exact truth; the products of the last processes must undergo fatty or other changes before they resemble tubercle.]
>
> 3. The tuberculoid metamorphosis is met with in newly-formed pathological tissues, in the old or physiological, and, lastly, in both at the same time, which is the common and characteristic occurrence. It affects the transitory elements composed of cells, or the permanent fibrous parts.
>
> 4. It consists in a cessation of the nutrient and formative processes, or a mortification, necrosis of the elements of tissues, with subsequent peripheric absorption of the fluid parts and the drying of those which are no longer nourished. This necrosis is caused by the accumulation of cell-elements, which compress the vessels of the part. [This last remark is very important in connection with the results of the microscopic examination of a number of cases of pneumonia, mentioned on page 412.]
>
> 5. These cells may be either newly formed, or result from an increased formation of the normal elements (epithelium, etc.), or may have an endogenous origin. The processes by which they arise have the characters belonging to simple hypertrophy, suppuration, cancerous or sarcomatous formations, or to the infiltrated products of typhoid fever and glanders.
>
> 6. All these processes show a marked local derangement of nutrition, especially altered exudation, and point back accordingly either to inflammation itself or analogous disorders, whether they originate in the irritation caused by local trouble, or are consecutive to constitutional causes, primary alterations of the blood. etc.
>
> 7. We have, therefore, an inflammatory, cancerous, typhoid, glanderous, and sarcomatous tuberculization, which are the same as far as the character of the

local process is concerned—that is, the metamorphosis of tissue—but differ more or less in the character of the *whole* process, whether the latter be regarded as attributable to local or general constitutional causes.

8. Tuberculosis is the entire morbid process, which includes the conditions of the local derangement of nutrition, with the changes in the exudation belonging thereto, as well as in the formation and transformation of cells. It finds its constant regular expression in tuberculization.

All tuberculization (tuberculoid metamorphosis) does not originate in tuberculosis. The latter may in its earlier stage (that of exudation, cell-formation) be present even if there be no tubercle. Tuberculosis we consider that morbid process which, when it pursues its usual course, always leads to tuberculization: while we ascribe cancer and sarcoma, which accidentally tuberculize, to an entirely different process, and should never give the name of tubercle to thickened caseous pus.

9. Inasmuch as tubercle arises from the accumulation in the tissues of a great variety of cells, which in the majority of cases are destroyed, *it is entirely without proper characteristic elements.* Of the remains of the cells, the shrivelled nuclei present the most constant external characters; we may therefore retain for these the name tubercle-corpuscle."

We are therefore justified in again asserting that the peculiarity of tubercle is a certain tendency, and any attempt to decide upon its real nature, by appealing to its anatomical characters alone, would be as futile as to predicate upon the external aspect of a number of new-born infants, their future mental, moral, or physical condition. They all contain germs of something good, bad, or indifferent, but time alone can show what their traits are to be. And, if in after years they become the pests of society, we must not trace the fallen condition of them all to original sin, but remember that they have been surrounded by various influences, and that, though reduced to the same low level, their downfall may be owing to various causes.